

NIAAA SPECTRUM

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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES • National Institutes of Health • National Institute on Alcohol Abuse and Alcoholism

FEATURE

LEVERAGING COLLABORATION TO ADDRESS ALCOHOL PROBLEMS



Alcohol consumption affects virtually every tissue and organ in the body and is associated with more than 200 diseases and injury-related conditions. For this reason, collaborative efforts across the National Institutes of Health (NIH) are critical. Research collaborations allow scientists from diverse fields of study to work together in new ways and to apply their unique strengths and resources toward a common problem.

“We’ve long recognized the cross-disciplinary nature of alcohol problems,” said National Institute on Alcohol Abuse and Alcoholism (NIAAA) Director George F. Koob, Ph.D. “While collaboration has always been an essential component of the research enterprise, this approach is particularly crucial to improving the prevention, diagnosis, and treatment of alcohol-related problems. Alcohol is relevant to many diseases and conditions, and building strategic relationships with our fellow NIH Institutes, Centers, and Offices [ICOs] is pivotal to advancing cross-cutting mission-related research areas and maximizing research resources.”

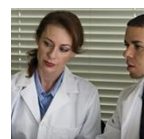
NIH-wide collaborations leverage the vast scientific resources and expertise across ICOs, enabling coordinated responses to complex problems that benefit from interdisciplinary or multidisciplinary approaches. Key areas of collaboration include:

Neuroscience Research

Neuroscience research has broad applications for the study of neurological and psychiatric disorders, including alcohol and other substance use disorders.

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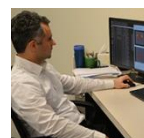


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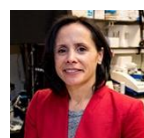


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NIAAA is one of 14 NIH ICOs that work together with the [NIH Office of the Director](#) on the [NIH Blueprint for Neuroscience Research](#), a collaborative framework that supports research on the nervous system. By pooling resources and expertise, the “Blueprint” identifies cross-cutting areas of research and confronts challenges too large for any single NIH component. Several areas of collaboration include drug discovery and development for central nervous system (CNS) disorders, neuroscience training, and research on neuroimmune interactions involved in the transition from healthy brain function to the onset and progression of CNS disorders.

As part of the [Brain Research through Advancing Innovative Neurotechnologies® \(BRAIN\) Initiative](#), NIAAA works with nine other NIH Institutes and Centers on a large-scale effort to accelerate neuroscience research by developing novel tools for studying the brain. Technological advances resulting from this initiative will facilitate innovative research that can enhance our understanding of a wide variety of brain disorders.

Within NIH’s [Intramural Research Program](#), scientists at NIAAA lead a collaboration of basic and clinical researchers who compose the [NIH Center on Compulsive Behaviors \(CCB\)](#). Compulsive behaviors, which include addiction, tics, and binge eating, are driven by shared neurocircuitry. Accordingly, the mission of the CCB is to understand the neurobiology of complex behaviors that result in compulsive and repetitive actions, and to develop and test new therapeutics aimed at alleviating or reversing them.

Pain Research

The relationship between alcohol and pain is complex. At high doses, alcohol dulls pain; however, long-term excessive drinking makes physical pain worse.

Understanding the relationship between alcohol and pain is an important area of research that may have implications for the opioid epidemic. NIAAA participates in the [Helping to End Addiction Long-term \(HEAL\) InitiativeSM](#), one avenue for supporting research in this area. The HEAL Initiative is an aggressive, NIH-wide effort to speed scientific solutions for both addiction and pain management to stem the national opioid public health crisis.

NIAAA also participates in the [NIH-Department of Defense-Veterans Affairs \(NIH-DoD-VA\) Pain Management Collaboratory](#), led by the [National Center for Complementary and Integrative Health](#), to build cost-effective large-scale clinical research capacity in military and veterans healthcare delivery organizations that focus on non-pharmacological approaches to pain management and other comorbid conditions, such as alcohol misuse.

Prevention and Treatment of Substance Misuse and Co-occurring Disorders

Alcohol misuse commonly co-occurs with other substance use and mental health disorders and plays a prominent role in suicides and in opioid and other drug overdoses. To support improvements in the prevention and treatment of substance misuse, NIAAA partners with the [National Institute on Drug Abuse \(NIDA\)](#) and the [National Cancer Institute \(NCI\)](#) through the [Collaborative Research on Addiction at NIH \(CRAN\)](#) to integrate resources and expertise to advance research on substance use, substance misuse, and addiction, as well as public health outcomes. A major initiative led by CRAN is the [Adolescent Brain Cognitive DevelopmentSM Study \(ABCD Study[®]\)](#), the largest long-term study of brain development and child health in the United States. NIAAA also collaborates with NIDA and the [National Institute of Mental Health \(NIMH\)](#) in exploring research strategies for addressing deaths due to substance misuse and suicide.

Effects of Alcohol on Health

Alcohol misuse contributes to nearly half of all liver disease deaths in the United States, and alcohol-associated liver disease (ALD) is now the leading cause of liver transplantation due to chronic liver disease. In addition to supporting basic, translational, and clinical research on potential ALD treatments, NIAAA is collaborating with the [National Institute of Diabetes and Digestive and Kidney Diseases](#) to enhance research on the shared mechanisms between alcohol-associated and non-alcohol-associated fatty liver disease and how one condition may exacerbate the other.

In the area of cancer research, NIAAA and NCI have partnered to stimulate research on the relationships between alcohol consumption and cancer risk and outcomes, including studies on the biological and behavioral mechanisms through which alcohol influences cancer risk. A better understanding of these relationships could lead to improved therapeutic approaches and preventive strategies.

Fetal alcohol spectrum disorders research represents another key area of collaboration. A sponsor and chair of the [Interagency Coordinating Committee on Fetal Alcohol Spectrum Disorders \(ICCFASD\)](#), NIAAA works with the [Eunice Kennedy Shriver National Institute of Child Health and Human Development](#), NIMH, and other federal partners to coordinate communication and collaboration across disciplines and federal agencies that address issues related to prenatal alcohol exposure.

Aging Research

One in ten adults ages 65 and older engage in binge drinking, and most older adults take a medication that could result in a harmful interaction with alcohol. NIAAA encourages research to increase the understanding of the effects of alcohol use on the brain and body of older adults, such as the link between advanced age and the risk for alcohol-induced brain damage and cognitive decline. Recently, NIAAA has partnered with the [National Institute on Aging](#) to expand research on the neurobiological mechanisms that underlie the influence of alcohol on the onset and progression of Alzheimer's disease and related dementias.

Overall, the adverse effects of alcohol misuse manifest throughout the body and across all segments of society. By collaborating with other NIH Institutes or federal agencies, NIAAA researchers bring diverse scientific knowledge and expertise to bear on these public health problems of mutual interest and concern, and thus multiply the value of crucial research resources. Through strategic relationships with NIH ICOs and other federal partners, NIAAA will continue to advance its mission to generate and disseminate fundamental knowledge about the effects of alcohol on health and well-being, and apply that knowledge to improve the diagnosis, prevention, and treatment of alcohol-related problems across the lifespan.

NEWS FROM THE FIELD

NIAAA SCIENTISTS HIGHLIGHT ALCOHOL-RELATED MORTALITY INCREASE IN THE UNITED STATES



A recent study by NIAAA scientists found that nearly 1 million people died from alcohol-related causes between 1999 and 2017. The analysis of yearly death certificate data revealed that the number of death certificates mentioning alcohol more than doubled from 35,914 in 1999 to 72,558 in 2017, a year in which alcohol played a role in 2.6 percent of all deaths in the United States. In 2017, liver disease (31 percent; 22,245 deaths) and overdoses on alcohol alone or with other drugs (18 percent; 12,954 deaths) accounted for 35,199 deaths, nearly half of the alcohol-related deaths in that year. People ages 45 to 74 had the highest rates of deaths related to alcohol, but the biggest increases over time were among people ages 25 to 34.

“The high rates among middle-aged adults are consistent with previous reports of increases in ‘deaths of despair,’ generally defined as deaths related to overdoses, alcohol-associated liver cirrhosis, and suicides, primarily among non-Hispanic whites,” said first author Aaron White, Ph.D., Senior Scientific Advisor

to the NIAAA Director. “However, in the current study, alcohol-related deaths were increasing among people in almost all age and racial and ethnic groups by the end of the study period.”

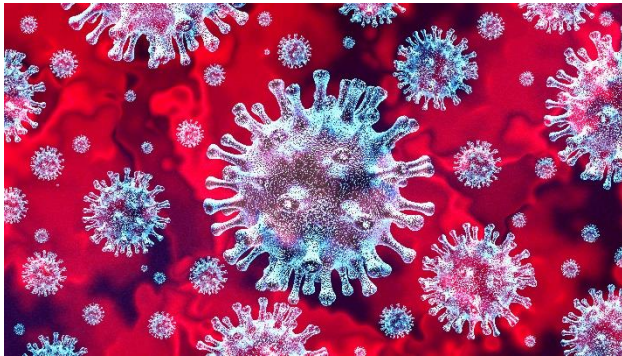
Rates of death involving alcohol also increased more for women (85 percent increase) than men (35 percent increase) over the study period, further narrowing once-large differences in alcohol use and harms between males and females.

“The findings come at a time of growing evidence that even one drink per day of alcohol can contribute to an increase in the risk of breast cancer for women,” said senior author Patricia Powell, Ph.D. “Women also appear to be at a greater risk than men for alcohol-related cardiovascular diseases, liver disease, alcohol use disorder, and other consequences. Our findings underscore that alcohol is a growing women’s health issue.”

Reference:

White, A.; Castle, I.-J.P.; Hingson, R.; and Powell, P. Using death certificates to explore changes in alcohol-related mortality in the United States, 1999–2017. *Alcoholism: Clinical and Experimental Research* 44:178–187, 2020. PMID: 31912524

SPOTLIGHT



ALCOHOL TREATMENT AND PHYSICAL DISTANCING

If you need alcohol treatment while practicing physical distancing, there are several professionally led treatment and mutual-support group options available to you:

Professionally Led Treatment

Many healthcare professionals and programs have offered telehealth alcohol treatment for years. These are phone or video sessions for talk therapy or medical care. Now, with the COVID-19 emergency, more providers are offering telehealth services.

Medicare and other insurers are expanding coverage of telehealth services as well. Check with your insurance company about coverage.

The National Institute on Alcohol Abuse and Alcoholism's (NIAAA) [Alcohol Treatment Navigator](#) can help you find telehealth alcohol treatment by healthcare professionals:

- » [Find treatment programs here](#) and filter for "telemedicine/telehealth." *Note: More programs are likely adding telehealth services during the COVID-19 emergency. If needed, search without the filter and call to check availability of telehealth services.*
- » [Find therapists with addiction specialties here](#) and filter for "video counseling." *Note: More therapists are adding telehealth services during the COVID-19 emergency. If needed, search without the filter and call to check availability of telehealth services.*
- » [Find doctors with addiction specialties here](#) and ask office staff whether they offer telehealth services.

Also, please note that an effective computer-based program can provide powerful support as well. [CBT4CBT™](#) is a set of web-based cognitive-behavioral therapy modules developed with NIAAA funding. It trains people in seven important skills to help them cut down or quit drinking. Any doctor or licensed therapist can prescribe it for you and monitor your progress.

Mutual-Support Groups

Mutual-support groups can be particularly helpful during this challenging time. A growing number of groups have online communities. These groups can vary widely, so it's important to try different ones to find a good fit.

The *Navigator* can help you find some [mutual-support groups](#) to consider.

In addition to support groups, people in recovery should also maintain a connection with their treatment counselor. While mutual help groups are an excellent source of support and encouragement, they are usually not run by professional clinicians. Some issues may require the help of a trained health professional.

Other Resources

If you'd like to get started with something right away, see this [list of online support groups, apps, and podcasts](#) from the American Society of Addiction Medicine.

Overall, regardless of where or how you seek treatment, it's important to look for approaches that are "evidence-based." This means the treatments are supported by large, well-designed studies. The *Navigator* will help you spot [signs of higher-quality care](#).

SPOTLIGHT



DISTINGUISHED INVESTIGATORS JOIN THE NIAAA DIVISION OF INTRAMURAL CLINICAL AND BIOLOGICAL RESEARCH

In 2019, two distinguished investigators joined NIAAA's [Division of Intramural Clinical and Biological Research \(DICBR\)](#).

Michelle Antoine, Ph.D., is a National Institutes of Health (NIH) Earl Stadtman Tenure-Track Investigator in the DICBR Intramural Research Program. The Stadtman program recruits highly talented and diverse early-career scientists. Dr. Antoine's research deciphers genetic and environmental factors that impair neurocircuit activity, leading to neurodevelopmental disorders. Her recent work on neuron signal activity led to important new insights into autism spectrum disorder. At NIAAA, Dr. Antoine is applying her basic research experience in neurocircuit function to neurodevelopmental comorbidities commonly seen in fetal alcohol spectrum disorders. Her research findings have been published in

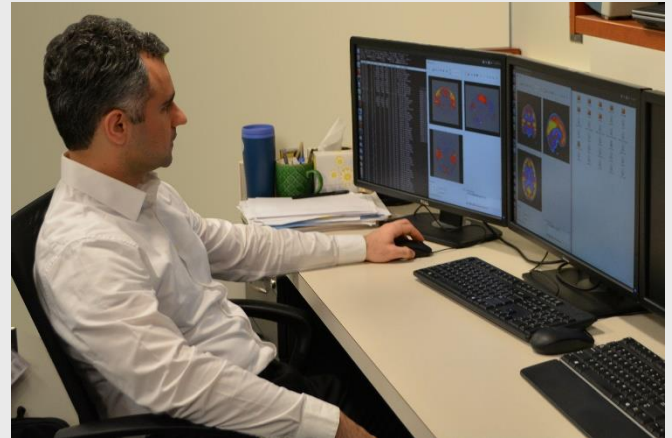
prominent scientific journals and highlighted in both the U.S. and international media. Dr. Antoine earned her doctorate from the Albert Einstein College of Medicine in New York and completed her postdoctoral training as a Miller Research Fellow in the Helen Wills Neuroscience Institute at the University of California, Berkeley. At NIAAA, she serves as Acting Chief of the Section on Neural Circuits in the [Office of the Scientific Director](#).



Paule Valery Joseph, Ph.D., was named one of NIH's 2019 Lasker Clinical Research Scholars. Dr. Joseph received a joint appointment with NIAAA and the National Institute of Nursing Research, where she leads the [Sensory Science and Metabolism Unit](#). The Lasker Clinical Research Scholars program allows early-stage clinician-scientists to conduct independent clinical and translational research at NIH. Dr. Joseph is collaborating with several DICBR investigators; these include Dr. Nora Volkow (NIAAA Laboratory of Neuroimaging) and Dr. Lorenzo Leggio (Section on Clinical Psychoneuroendocrinology and Neuropsychopharmacology, a joint NIAAA-National Institute on Drug Abuse laboratory). A focus of Dr. Joseph's research at NIAAA is to explore, at the neurobiological level, how senses such as smell and taste are involved in cues that trigger craving for alcohol, a diagnostic feature of alcohol use disorder. Dr. Joseph received her bachelor of science in nursing from the College of New Rochelle, New York, and her doctorate in nursing with a focus on genomics from the University of Pennsylvania.

NIAAA@WORK

LABORATORY OF NEUROIMAGING



Ehsan Shokri Kojori, Ph.D., a Research Fellow in the NIAAA [Laboratory of Neuroimaging](#), seeks to understand how autonomic activity that controls vital body functions, such as blood pressure and breathing, affects brain networks and how that information relates to substance misuse and neuropsychiatric disorders. His work involves looking deep into the human brain using tools such as magnetic resonance imaging (MRI) and positron-emission tomography (PET) imaging. On the left, Dr. Shokri Kojori is pictured with an individual being prepared for an MRI scan, which creates detailed images of the brain. On the right, he reviews brain maps created from several MRI and PET scans. This information allows him to characterize the associations between brain structure, chemistry, and function.

NOTEWORTHY



MORE NIAAA FACTSHEETS NOW AVAILABLE IN SPANISH

NIAAA recently released the following new additions to its series of Spanish-language factsheets:

- [Recuerdos interrumpidos: lagunas mentales inducidas por el alcohol](#), a translation of [Interrupted Memories: Alcohol-Induced Blackouts](#)
- [Las mujeres y el alcohol](#), a translation of [Women and Alcohol](#)
- [Resaca](#), a translation of [Hangovers](#)

Other NIAAA materials in Spanish are available to view and download at <https://www.niaaa.nih.gov/publicaciones-en-español>.

NOTEWORTHY



THE 24TH MARK KELLER HONORARY LECTURE

Laura E. Nagy, Ph.D., delivered NIAAA's [24th annual Mark Keller Honorary Lecture](#) on Tuesday, January 28 at the National Institutes of Health. The title of her talk was "Inflammation and Cell Death in Alcohol-Associated Liver Disease."

A world-renowned alcohol scientist, Dr. Nagy's work has greatly advanced our understanding of alcohol's impact on organ and immune system interactions. Notably, she has made seminal contributions to defining the innate immune system's role in the progression of alcohol-associated liver disease (ALD). She and her colleagues also have done pioneering work on alcohol's impact on adipose tissue and on the interaction between adipose tissue and the liver in the development of ALD.

In her talk, Dr. Nagy discussed the recent discovery in her laboratory that the treatment of mice with small, specific-sized hyaluronic acid

of 35 kD (HA35) can directly prevent ethanol-induced liver injury and protect the barrier function of the intestine. She summarized a series of in vitro and in vivo experiments that identified an essential miR181b-3p–importin α 5 regulatory axis in hepatic macrophages that contributed to the sensitization of Kupffer cells to TLR4-mediated cytokine production via enhanced accumulation of the p65 subunit of NF κ B to the nucleus. Dr. Nagy explained how these mechanistic insights could be translated into new treatments for ALD. She also reviewed what we know about non-canonical functions of cell

death proteins in murine models of non- and alcohol-associated fatty liver and steatohepatitis, as well as commented on their potential use as biomarkers.

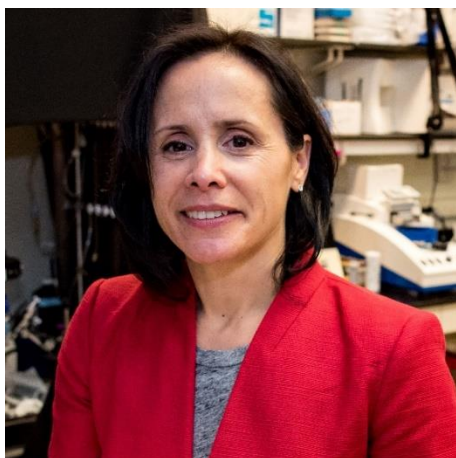
Dr. Nagy is currently a professor of molecular medicine at the Cleveland Clinic Lerner College of Medicine at Case Western Reserve University, where she also serves as an adjunct professor of nutrition. Dr. Nagy is also on staff in the departments of inflammation and immunity, and gastroenterology and hepatology at the Cleveland Clinic.

To view Dr. Nagy's talk, please visit the [NIH videocast website](#).

5 QUESTIONS WITH. . .

VERONICA ALVAREZ, PH.D.

Senior Investigator, NIAAA Laboratory on Neurobiology of Compulsive Behaviors, NIH Intramural Research Program



1 As Chief of NIAAA's Laboratory on Neurobiology of Compulsive Behaviors (LNCB), how would you describe your lab's work to non-scientists?

[Our laboratory](#) focuses on understanding how alcohol and other substances change the brain and the connections among brain cells, or neurons. We think that some of the changes associated with alcohol use may explain why a subset of individuals develop a compulsion to consume alcohol and display a strong drive to seek it despite the negative consequences.

We explore an essential question: why are some people more prone than others to developing alcohol and other substance use disorders? Our hypothesis is that vulnerability lies within the patterns of brain wiring. Multiple factors play a critical role in determining how the brain is connected and wired: genes, developmental processes, environmental factors, previous experiences, stress, etc. We are very interested in understanding the vulnerability factors underlying the compulsive aspect of behavior, in part because discoveries in this field would be critical to improving treatment outcomes for people with alcohol and other substance use disorders.

2 Can you summarize some of your lab's significant accomplishments?

Recently, our team discovered a causal link between two factors known to be important in alcohol use disorder (AUD). The first factor is low sensitivity to the sedative effects of alcohol; research suggests that individuals with a low sensitivity to alcohol have a higher likelihood of developing AUD. In animal models, this can be measured as an enhancement in alcohol-induced stimulation. The other factor is lower levels of dopamine receptors—D2 receptors—within the basal ganglia, a brain region that plays a critical role in the rewarding, or pleasurable, effects of alcohol and other substances and in the formation of habitual substance use. Individuals with AUD tend to have lower levels of dopamine D2 receptors.

Using a mouse model, the LNCB team found that lowering the levels of D2 receptors in the brain was sufficient to increase alcohol-induced stimulation and decrease alcohol sedation. We also showed that lower levels of D2 receptors cause an increase in the signaling and activity of another major dopamine receptor type—the D1 receptor. Increased activity of dopamine D1 receptors contributes to the stimulating effects of alcohol in these animal models and their increased preference for alcohol over natural rewards.

3 Collaboration has been a hallmark of your career—in fact, your research receives support from multiple NIH Institutes, and you currently direct the Center on Compulsive Behaviors within the NIH Intramural Research Program. Why is collaboration so central to your work?

In a sense, because I conduct basic research on the brain, it has been a natural development to collaborate across neuroscience disciplines. In fact, the National Institute of Neurological Disorders and Stroke (NINDS) has provided additional funds for my program since I started at NIAAA more than 10 years ago. In 2017, I was privileged—and felt it was very much a once-in-a-lifetime opportunity—to be invited to help start and direct the collaborative NIH Center on Compulsive Behaviors.

For me, scientific collaboration feels more like a need than a choice: I work so much better in teams! I get most of my best ideas from talking and discussing with others. I find it very stimulating and enriching to work as part of a team.

4 You have been honored as an outstanding mentor and were distinguished by NIH as an “agent of change” for greater diversity within the scientific community. What is the importance of these issues for you?

Working alongside the fellows and trainees is the most rewarding part of my work. Watching them learn and overcome challenges is inspiring. And I learn so much from them. I consider mentoring and training the next generation of scientists to be both an incredible privilege and a responsibility. I owe so much to my own mentors that I feel this is a way to give back.

Also, I am convinced that in order to solve most of the problems we face, we must bring together people with diverse viewpoints, disciplines, expertise, and cultural and socioeconomic backgrounds. In my experience, diverse teams of individuals are really effective in science.

5 You moved to the United States from Argentina after earning your Ph.D. at the University of Buenos Aires. In what ways has the experience of that transition shaped your outlook and career?

As I mentioned before, I truly believe that diversity has a unique role to play in science and our society. My background shaped my view of the world, and my rich, diverse training has given me unique tools. In Argentina, people have fewer resources, so we need, by necessity, to be creative and make things work. I learned two important lessons from a very young age: you have to make it work with what you have, and you need to go get whatever you are missing; you cannot just wait for it. Also, I had very committed teachers and mentors and an incredibly talented group of peers with whom I am still in touch.

ABOUT US

NIAAA Spectrum is NIAAA's triannual webzine. With engaging feature articles, short news updates, and colorful graphics, *NIAAA Spectrum* offers accessible and relevant information on NIAAA and the alcohol research field.

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